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Antipyrin in Rheumatism; its Value and Mode of Action.

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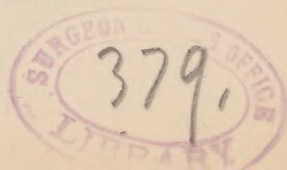
ANTIPYRIN IN RHEUMATISM; ITS VALUE AND MODE OF ACTION.

During the last few months numerous writers in Germany and France have described the good effects of antipyrin in acute rheumatism. It has been said of it that it relieves the pain and allays the fever as quickly as does the salicylate of soda, and that under its influence the cutaneous redness over the affected joints, and their swelling, gradually but soon disappears.

All of these statements I can confirm by my experience during the last four months in some twenty cases.

I have used antipyrin in acute cases, also in those that were subacute and in the acute exacerbations of those that were chronic. I noticed early that the greatest and most rapid improvement was obtained in cases in which there was a rise of temperature above the normal.

The first case in which I used antipyrin was one of chronic rheumatism in which there was, at the time, an acute exacerbation. The patient's stomach was so irritable that very little was retained by it. Enough of salicylic acid or of the salicylates could not be given to produce an impression on the disease. I therefore tried as an experiment a single dose of antipyrin, of twenty grains, at bed time. Soon after taking the medicine the pains, which were uniformly much more severe at night than during the day, were eased. The patient breaking into a profuse perspiration, fell asleep and passed the first restful night for some weeks. After a few days under this treatment her fever disappeared and she was almost free from pain. When the fever was wholly wanting it was noticed that the antipyrin ceased to ease the



pain that remained, and did not relieve the chronic stiffness and swelling of the joints. As often, however, as the temperature rose the antipyrin acted well. I have met with similar results in the treatment of three other cases of chronic rheumatism. No relief to the pain, swelling and other symptoms of inflammation was obtained in a case of gonorrhœal rheumatism in which one ankle, one knee and the joints of the fingers were much swollen and exceedingly painful. There was in this case at the time no fever.

As an illustration of the action of antipyrin in acute cases, I will cite the history of a young man recently dismissed from Mercy Hospital, apparently cured. He had been sick with a sharply acute and quite severe attack of rheumatism for ten days, when he entered the hospital. During that time most of the large joints had been in turn affected. When first seen by me his temperature was 103° ; his pulse quick, bounding, full, but compressible; his skin moist, with moderate perspiration; his countenance indicated pain and distress. At the time the pain was almost wholly limited to the left knee and right shoulder and elbow. All these joints were considerably swollen, and the skin over the knee was very slightly reddened. There were no evidences of endo- or pericarditis. Appetite was completely wanting, but thirst was much increased. The bowels were constipated. The urine was somewhat scant and highly colored. Sleep of more than momentary duration had been impossible for many days. In a word, the patient at the moment presented the symptoms characteristic of a typical case of acute rheumatism. As it was one of the earliest cases of acute rheumatism that I treated wholly with antipyrin, I ordered at first the administration of a powder containing twenty grains of the drug only night and morning. The following afternoon he reported that soon after taking the medicine he slept, and for three

or four hours was free from pain, but as the influence of the drug wore off the pain returned. His temperature had then lowered, but was still considerably above normal. I now ordered the antipyrin powders given three times daily instead of twice. Two days later the patient looked much better, and described himself as almost free from pain; the cutaneous redness over the knee was gone, and all the joints were less swollen, but still stiff and somewhat painful on attempted motion. The temperature for the most part during the preceding twenty-four hours was normal; twice it rose slightly. The frequency of the administration of the antipyrin was left to the judgment of the house physician; the directions being to administer the drug whenever the temperature rose or an access of pain occurred. Following this plan, he received during the next two days two powders daily. He was entirely comfortable so long as quick and violent movements were not attempted. For eighteen hours there had been no abnormal temperature. The swelling of the joints was much less, and freedom of motion much greater. The case progressed steadily in a favorable manner, and all stiffness and pain disappeared during the next week. The antipyrin was continued for several days after all fever was gone. No other medicine was administered after its discontinuance, the patient simply being guarded against adverse atmospheric influences.

In the other acute cases in which I have tried antipyrin I have been most pleased with the readiness with which it relieved pain and lessened fever. In some instances the improvement was more marked and more rapid than in the case I have just sketched; in others it was somewhat slower, but always decided. I feel confident that, so far as a limited number of cases will permit one to determine, antipyrin can be said to be as efficacious as the salicylates. Being at first impressed with the thought that the relief obtained in rheumatism was due to the antipy-

retic effects of the drug, I substituted for it salicylic acid as soon as the temperature became normal; as, however, experience showed that the efficacy of antipyrin did not depend upon this property, I continued its use, as improvement took place, in lessened doses and less frequently until a cure was established.

In the hospital cases most recently treated the drug has been used in fifteen grain or gram doses, administered at the height of the disease every four hours, diminishing the frequency of its repetition as improvement occurred. It has seemed to me that I obtained more satisfactory results in my private patients to whom I gave it in larger, twenty grain, doses, four times daily, when the disease was at its height, and to whom, during the period of improvement, it was given in smaller doses, but not at first less frequently. From sixty to ninety grains (four to six grams) daily are recommended usually by those who have employed antipyrin in rheumatism.

The advantage of antipyrin over the salicylates consists chiefly in its less nauseating properties, its less liability to provoke vomiting, headache, and noises in the ears. Not unfrequently a patient is found who can not take the salicylates in efficient doses. While trying antipyrin, both in rheumatism and in other febrile diseases, I have found only one or two persons who rejected it; and a few others, whose stomachs were irritable, who complained of slight nausea immediately after taking it. These effects are, however, much less frequently produced by it than by the salicylates. It can also be given efficiently, when necessary, by the rectum or subcutaneously.

The only ill effect that is likely to result from the use of antipyrin is the so-called "antipyrin rash." This is seen only in a very small proportion of the cases treated with it. Two or three cases of fatal collapse have been reported, occurring in typhoid patients, after taking antipyrin. At the most, how-

ever, this is an exceedingly rare accident, and it is questionable even if, in the cases referred to, the accident was due to the antipyrin. Ringing in the ears has been reported as occurring, but so seldom that it need not be looked for when the usual doses are used.

Others have found, very rarely, a case of acute rheumatism in which no relief could be obtained from the antipyrin treatment. The same can be said, however, of the usual salicylate treatment.

The use of the drug does not appear to influence the frequency of the occurrence of heart complications, and their existence is not a contra-indication to its employment.

It is impossible, from what we yet know of the nature of rheumatism and of the physiological action of antipyrin, to explain thoroughly its therapeutic action. The perspiration which very uniformly follows its administration, and in rheumatism seems to accompany the diminution of pain, is probably due to relaxation of the cutaneous vessels, such as has been observed by Beyer¹ and others, and which naturally would feed and stimulate the cutaneous glands. It has been shown that the peripheral vessels dilate under the influence of antipyrin, the arteries dilating when large doses are administered, and only the veins and capillaries when smaller ones are employed. Whether this change of calibre is due to vaso-motor influence or not is undecided, some claiming that the change is brought about by the direct action of the drug upon the vessels, since similar changes take place in isolated organs;² others claiming the reverse to be true.³

Antipyrin, when mixed with blood, does not cause a change of color or destruction of the corpuscles,

¹ "The Influence of Kairin, Thallin, Hydrochinon, Resorcin and Antipyrin on the Blood and Blood-vessels." By H. G. Beyer, *Am. Journ. Med. Sci.*, April, 1886.

² Quireilo and Coppola. See article by Beyer, *Am. Journ. Med. Sci.*

³ Ausseroff, *Therapeutic Gazette*, May 15, 1886.

as does kairin, thallin, resorcin, and probably anti-febrin.⁴

Possibly its antipyretic properties are to be explained by the vascular changes which it produces, since they would contribute to increase the radiation of bodily heat. This is the explanation offered by Bettelheim,⁵ Auseroff and Beyer. Arduin thinks the diminution in temperature is due to an influence exerted upon the thermogenic nerve-centres. During the last month P. J. Martin⁷ has published the results of experiments which show that, almost uniformly, heat production is diminished by antipyrin, and heat dissipation is very much increased. It thus would seem to be an ideal antipyretic. In the small proportion of cases in which heat production was not diminished, heat dissipation was so far in excess that the bodily temperature was lowered. Several observers have noted that under the influence of antipyrin the surface temperature rises while the internal temperature of the body falls.⁸

Its power of allaying pain in rheumatism is probably not dependent upon these vascular changes or the apyrexia produced by it, but upon a direct action on the nervous structures of the body. Antipyrin, though apparently most efficacious in rheumatic fever and least in muscular rheumatism; still, even in the latter, often acts beneficially. In many painful disorders purely neuralgic in character it gives the most prompt relief; for example, to the sharp neuralgic pains of locomotor ataxia. Ungar,⁹ T. S. Robertson,¹⁰ and others, say it is efficacious in migraine. Germain Sée¹¹ has witnessed its power of relieving

⁴ "De l'antipyrin contre la douleur." Par Germain Sée, *Le Bulletin Médical*, April 20, 1887.

⁵ Bettelheim, *Med. Jahr. K. K. Ges. d. Aerzt.*, ii, iii, 1886.

⁷ "Modern Antipyretics." By P. J. Martin, *Therapeutic Gazette*, May 16, 1887.

⁸ See Beyer, *Am. Journ. Med. Sci.*

⁹ Ungar. *Centralblatt f. d. Gesamte Therapie*, January, 1887.

¹⁰ "Antipyrin in Migraine, Pyrexia, etc." T. S. Robertson, *N. Y. Med. Record*, May 7, 1887.

¹¹ See above, *Le Bulletin Médical*.

pain in other forms of neuralgia, and in gout, lumbago and sciatica.

The fact that there was in these diseases no common pathological effect except that of pain, led the last writer to study particularly its action upon the nervous system. The results of his experiments he reported to the French Academy of Sciences on the 18th of April of this year. When injected subcutaneously in dogs three kinds of phenomena were observed: In the first place, a notable diminution of sensibility was observed, a true analgesia of the limb injected; sometimes, also, of the opposite one. In the second place, electric excitation of the sciatic nerve produced in the muscles of the opposite side only very feeble contractions, which points to diminished sensibility and reflex power in the spinal cord. In the third place, when antipyrin was introduced into the circulation of an animal except into one limb, the vessels of which were ligated, it was found that throughout the body the muscles contracted slowly and with difficulty, while those of the ligated limb contracted with their wonted vigor. It is evident, therefore, that antipyrin also affects the muscles; or more properly, perhaps, the nerve-endings in the muscles. Analgesic effects have been frequently noted by others. Large doses administered to animals cause convulsions, both clonic and tonic. Lessening of the reflexes, also, has been observed by others, as, for instance, by Arduin.¹² This last author, as well as Coppola,¹³ thinks that the brain is influenced by the drug, since, when convulsions are produced by it, their severity is much diminished if the brain is separated from the cord.

Antipyrin does not affect the respiratory movements, although the frequency of respiration in fever diminishes as the temperature falls under its influence. As ordinarily administered, the rhythm and strength

¹² Arduin, *Therap. Gazette*, October 15, 1885.

¹³ Coppola, *Therapeutic Gazette*, October 15, 1885.

of the heart's action are not influenced. Beyer has shown by physiological experiments that when it exists in small amounts in the circulatory fluids, it causes an increase of work performed by the heart, while in large doses the contrary effect is produced. Some have also noted increased force in the heart's action, while others have observed a diminution in it. This discrepancy is probably due to the size of the dose administered.

The drug is eliminated by the urine, and can be found in it two hours after administration, and usually for thirty-six to forty-eight hours afterwards."

The following conclusions are, I think, justified by our present knowledge of antipyrin in the treatment of rheumatism: 1. It is as efficacious as the salicylate of soda, producing similar therapeutic results, and is less nauseous than the latter, and does not produce headache or ringing of the ears. 2. Usually it acts most efficiently in the most frankly acute cases. 3. Besides reducing, by its antipyretic properties, the fever, and also the pain, which many antipyretics relieve, it reduces the pain by acting directly upon the nervous system.

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